Testimony
Before the Subcommittee on Criminal Justice,
Drug Policy and Human Resources
Committee on Government Reform
United States House of Representatives

The Role of the HHS Office for Human Research Protections in Protecting Human Research Subjects

Statement of

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For Release on Delivery
Expected at 2:00 p.m.
Tuesday, March 7, 2006

Mr. Chairman and Distinguished Members of the Subcommittee, thank you for inviting me here today to discuss the Department of Health and Human Services' (HHS') Protection of Human Subjects Regulations, particularly as they relate to human cloning and embryonic stem cell research.

These HHS regulations are designed to protect the rights and welfare of all who participate in research studies that are conducted or supported by HHS. They are based in large part on three fundamental ethical principles for human subjects research – respect for persons, beneficence, and justice. These principles were identified in the *Belmont Report,* written by the congressionally created National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in 1978.

In 1991, the core HHS regulations for human subjects protections – codified at subpart A of 45 CFR part 46 – were extended to14 other Federal departments and agencies, when those entities joined HHS in adopting a uniform set of regulations that are identical to HHS' subpart A. This standardization of protections is known as the Federal Policy for the Protection of Human Subjects, and generally referred to as the "Common Rule."

The protection of human subjects in research studies is a priority for HHS, and it is the mission of the Office for Human Research Protections (OHRP) to support, strengthen and provide leadership to the Nation's system for protecting volunteers in research that is conducted or supported by HHS.

HHS Regulations

The HHS regulations encompass all research involving human subjects that is conducted or supported by HHS. By signing an assurance of compliance with OHRP, an institution pledges to conduct its HHS-funded or -supported research in accordance with these regulations. An institution also may voluntarily extend these HHS protections to all its human subjects research, regardless of funding source; and many institutions choose to do so.

In addition to assurances of compliance, the HHS regulations also stipulate a number of other requirements, for which the institution and its institutional review board (IRB) are responsible. These include but are not limited to:

- IRB membership;
- Criteria for the IRB to review and approve or disapprove research;
- IRB procedures;

- Suspension or termination of IRB approval of research;
- Documentation of informed consent; and
- Use of Federal funds.

Two requirements are fundamental to compliance with the regulations:

- First, the research institution must designate one or more IRBs with responsibility for reviewing human subjects research. Among an IRB's many duties is its duty to ensure that the risks to subjects are reasonable in relation to any anticipated benefits, and in relation to the importance of the knowledge that may reasonably be expected to result. (45 CFR 46.111(a)(2))

- Second, the IRB must ensure that the research meets the provisions for informed consent of the subject. These provisions are designed to allow potential subjects to be made fully aware of both the risks as well as reasonably foreseeable benefits of involvement with the study.

Over the years, HHS has adopted additional research protections for various populations considered to be particularly vulnerable. These are in addition to the basic protections for human subjects in subpart A. The additional protections include:

- Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research (codified at Subpart B of the regulations);
- Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects (codified at Subpart C); and
- Protections for Children Involved as Subjects in Research (codified at Subpart D).

IRB Review and Approval

Much research is an inquiry based on a hypothesis whose outcome cannot be known in advance. Although some research studies offer subjects the prospect of direct benefit and others do not, an important feature of all research is that individual human subjects may or may not benefit from participation.

For example, when comparing two clinical interventions, researchers must be uncertain about which intervention will be found superior. This is known as "clinical equipoise" and is based on the ethical principles of beneficence and justice, as explicated in the *Belmont Report*, which I mentioned earlier. Some research studies offer individual subjects the prospect of direct benefit and others do not. But it is always important for subjects to know – before taking part in the study – that they may or may not experience any direct benefit from their participation.

As part of an IRB's review, the IRB must make several determinations before it can approve the research. Primary among these is need to determine if the "risks to subjects are reasonable in

relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result" (45 CFR 46.111(a)(2)).

When research studies offer no prospect of direct benefit to research subjects, IRBs must consider whether the potential benefits to society justify the risks to the individual subjects. For these studies, including some research involving human embryonic stem cells, the expected benefits would often occur in the future and would be of help to others who suffer from the same disease or condition as the subject participating in the research.

Informed Consent

At the heart of the human-subject protections system that governs HHS-funded or -conducted research is the requirement relating to informed consent. The investigator must seek a potential subject's informed consent, according to the requirements laid out in the regulations. And the investigator's method for obtaining this informed consent must be approved by the IRB before it can be applied. The only exception to this requirement for informed consent is if the IRB has determined that specified waiver criteria have been met (45 CFR 46. 116(d)).

The requirement for informed consent under the HHS regulations embodies the ethical principle of respect for persons, and further protects the rights and welfare of research subjects. In seeking informed consent, HHS regulations require that investigators do so only under circumstances that provide the prospective subject with sufficient opportunity to consider whether or not to participate, and that minimize the possibility of coercion or undue influence.

As part of the informed consent process, the prospective research subject must be given sufficient information about a research study to make an informed decision about whether to participate in the research, or not. If the research study does not offer subjects the possibility of direct benefit, this must be clearly stated in the informed consent process.

For example, if a research study that involves identifiable human cell lines is not intended to offer donors with the prospect of direct benefit, then prospective donor-subjects would need to be informed of this during the informed consent process, unless the requirement for informed consent had been waived by the IRB.

OHRP Guidance on Research Involving Stem Cells

The Office for Human Research Protections has provided guidance to help ensure that investigators and IRBs understand how the HHS regulations apply to research involving human embryonic stem cells, germ cells, and stem cell-derived test articles. A copy of this guidance is included with my written statement for the Subcommittee's consideration and is also available online at http://www.hhs.gov/ohrp/humansubjects/guidance/stemcell.pdf.

In essence, this guidance indicates when such research does and does not generally meet the HHS definition of human-subjects research. Under the HHS regulations, "human subject" means a living individual about whom an investigator conducting research obtains: (1) data through intervention or interaction with the individual; or (2) identifiable private information. OHRP

considers that neither of these definitions is met with research involving human embryonic stem cells, germ cells, and stem cell-derived test articles – as long as the investigator has not obtained data about an individual through a research intervention or interaction, and cannot readily ascertain the identity of the individual from whom the human material was obtained.

For example, if an investigator carrying out research using established human cell lines cannot readily ascertain the identity of the donor or donors of the original cell line, then the study would not be considered human subject research and would not be governed by the HHS human subject protection regulations. Because of this, the institution's IRB would not be required to review this type of research.

However, some research may use established human cell lines where the donor or donors may be readily identified by investigators, or may involve the obtaining of data through research interventions or interactions with individuals. In these cases, the research is considered to involve human subjects, it would be governed by the HHS regulations, and IRB review and approval would be required for the research to proceed.

Finally, I would like to emphasize that the stem cell research conducted at Seoul National University by Dr. Woo Suk Hwang, which provided the impetus for this hearing, was neither conducted at nor supported by HHS. Quite apart from the issues of fraud and abuse, such research could not have been conducted or supported by HHS under Federal law in the United States. Dr. Hwang's research involved attempts to create new human embryonic stem cells lines (solely for research purposes) through the process of somatic cell nuclear transfer, sometimes called human cloning. HHS is specifically prohibited by law from supporting "research in which a human embryo or embryos are destroyed," as well as from supporting "the creation of a human embryo or embryos for research purposes," and that law (most recently P.L. 109-149, Title V, Section 509) defines human embryo to specifically include embryos created by cloning. As it was not conducted at or supported by HHS, and does not appear to have been conducted at an institution that voluntarily agreed to comply with the HHS regulations for all human subjects research conducted at the institution, Dr. Hwang's research was therefore not subject to any of the regulatory protections that I have discussed throughout this statement.

Conclusion

In conclusion, through this system of IRB review and informed consent, the HHS regulations protect the rights and welfare of human subjects, while enabling investigators to conduct important, ethical research that is of benefit to society.

Thank you for you attention, and I would happy to answer any questions you may have.